PALM INTRANET

Day : Tuesday
Date: 4/13/2004

Time: 13:01:14

Inventor Name Search

Enter the **first few letters** of the Inventor's Last Name.
Additionally, enter the **first few letters** of the Inventor's First name.

Last Name	**First Name**	
Zannis	Vassilis	Search

To go back use Back button on your browser toolbar.

Back to PALM | ASSIGNMENT | OASIS | Home page

h e eb cg b e f e

Refine Search

Search Results -

Term	Documents
(3 NOT 4).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	11
(L3 NOT L4).PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD.	11

Database:
US Pre-Grant Publication Full-Text Database
US Patents Full-Text Database
US OCR Full-Text Database
EPO Abstracts Database
JPO Abstracts Database
Derwent World Patents Index
IBM Technical Disclosure Bulletins

Search:

Refine Search

Recall Text Clear Interrupt

Search History

DATE: Tuesday, April 13, 2004 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; THES=ASSIGNEE; PLUR=YES; OP=AND			
L5	L3 not L4	11	L5
L4	L3 and (hypertriglyceridemia or cholesterol)	7	L4
L3	(apoE3) same (vector or plasmid)	18	L3
L2	(truncated) same (apoE3 or apoE?)	6	L2
L1	Zannis-Vassilis-I$.in.	3	L1

END OF SEARCH HISTORY

```
### Status: Path 1 of [Dialog Information Services via Modem]

### Status: Initializing TCP/IP using (UseTelnetProto 1 ServiceID pto-dialog)
Trying 31060000009999...Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:
 ******** HHHHHHHH SSSSSSSS?
### Status: Signing onto Dialog
 ********
ENTER PASSWORD:
 ******** HHHHHHHH SSSSSSSS? ********
Welcome to DIALOG
### Status: Connected


Dialog level 04.02.00D

Last logoff:  09apr04 15:22:04
Logon file001 13apr04 12:25:17
           *** ANNOUNCEMENT ***
                     ***
--File 654 - US published applications from March 15, 2001 to the
present are now online.  Please see HELP NEWS 654 for details.

                     ***
--File 581 - The 2003 annual reload of Population Demographics is
complete. Please see Help News581 for details.

                    ***
--File 990 - NewsRoom now contains February 2003 to current records.
File 992 - NewsRoom 2003 archive has been newly created and contains
records from January 2003. The oldest months's records roll out of
File 990 and into File 992 on the first weekend of each month.
To search all 2003 records BEGIN 990, 992, or B NEWS2003, a new
OneSearch category.
                     ***
--Connect Time joins DialUnits as pricing options on Dialog.
See HELP CONNECT for information.
                     ***
                     ***
--SourceOne patents are now delivered to your email inbox
as PDF replacing TIFF delivery. See HELP SOURCE1 for more
information.
                     ***
--Important news for public and academic
libraries.  See HELP LIBRARY for more information.
                     ***
--Important Notice to Freelance Authors--
See HELP FREELANCE for more information
                     ***
NEW FILES RELEASED
***AeroBase (File 104)
***DIOGENES: Adverse Drug Events Database (File 181)
***World News Connection (File 985)
***Dialog NewsRoom - 2003 Archive (File 992)
***TRADEMARKSCAN-Czech Republic (File 680)
***TRADEMARKSCAN-Hungary (File 681)
***TRADEMARKSCAN-Poland  (File 682)
                     ***
UPDATING RESUMED
                     ***
RELOADED
***Medline (Files 154-155)
***Population Demographics -(File 581)
***CLAIMS Citation (Files 220-222)
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REMOVED
                    ***

      >>> Enter BEGIN HOMEBASE for Dialog Announcements <<<
      >>>    of new databases, price changes, etc.      <<<
                    ****
KWIC is set to 50.
HILIGHT set on as '*'
*
*
* ALL NEW CURRENT YEAR RANGES HAVE BEEN * * *
* * * INSTALLED   * * *

File   1:ERIC  1966-2004/Mar 31
       (c) format only 2004 The Dialog Corporation

      Set  Items  Description
      ---  -----  -----------
Cost is in DialUnits
?b 155, 5, 73
       13apr04 12:25:28 User259876 Session D610.1
            $0.33    0.094 DialUnits File1
     $0.33  Estimated cost File1
     $0.05  TELNET
     $0.38  Estimated cost this search
     $0.38  Estimated total session cost   0.094 DialUnits


SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R)  1966-2004/Apr W1
        (c) format only 2004 The Dialog Corp.
*File 155: Medline has been reloaded. Accession numbers
have changed. Please see HELP NEWS 154 for details.
  File   5:Biosis Previews(R)  1969-2004/Apr W1
        (c) 2004 BIOSIS
  File  73:EMBASE  1974-2004/Apr W1
        (c) 2004 Elsevier Science B.V.

      Set  Items  Description
      ---  -----  -----------
?s (truncated) (s) (apoE3 or apoE-3 or apoE?)
          190559  TRUNCATED
            1187  APOE3
               1  APOE-3
           20059  APOE?
      S1     253  (TRUNCATED) (S) (APOE3 OR APOE-3 OR APOE?)
?s s1 (s) (vector or plasmid or adenovirus or adenoviral)
             253  S1
          266760  VECTOR
          185000  PLASMID
           68597  ADENOVIRUS
           15865  ADENOVIRAL
      S2      22  S1 (S) (VECTOR OR PLASMID OR ADENOVIRUS OR ADENOVIRAL)
?s s2 and (cholesterol or hypertriglyceridemia)
              22  S2
          371828  CHOLESTEROL
           17419  HYPERTRIGLYCERIDEMIA
      S3      14  S2 AND (CHOLESTEROL OR HYPERTRIGLYCERIDEMIA)
?rd
...completed examining records
      S4       6  RD (unique items)
?t s4/3,k/all

 4/3,K/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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```

15697086 PMID: 12576523

Hyperlipidemia in APOE2 transgenic mice is ameliorated by a truncated apoE variant lacking the C-terminal domain.

Gerritsen Gery; Kypreos Kyriakos E; van der Zee Andre; Teusink Bas; Zannis Vassilis I; Havekes Louis M; van Dijk Ko Willems

Department of Human Genetics, Leiden University Medical Center, The Netherlands.

Journal of lipid research (United States) Feb 2003, 44 (2) p408-14, ISSN 0022-2275 Journal Code: 0376606

Contract/Grant No.: HL 68216; HL; NHLBI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Familial dysbetalipoproteinemia associated with the apolipoprotein E2 (*APOE2*) genotype is a recessive disorder with low penetrance. We have investigated whether additional expression of full-length *APOE3*, *APOE4*, or a *truncated* variant of *APOE4* (*APOE4*-202) can reduce *APOE2*-associated hyperlipidemia. This was achieved using *adenovirus*-mediated gene transfer to mice transgenic for human *APOE2* and deficient for endogenous *Apoe* (*APOE2*.*Apoe*-/- mice). The hyperlipidemia of *APOE2*.*Apoe*-/- mice was readily aggravated by *APOE3* and *APOE4* overexpression. Only a very low dose of *APOE4* *adenovirus* was capable of reducing the serum *cholesterol* and triglyceride (TG) levels. Expression of higher doses of *APOE4* was associated with an increased VLDL-TG production rate and the accumulation of TG-rich VLDL in the circulation. In contrast, a high dose of *adenovirus* carrying *APOE4*-202 reduced both the *cholesterol* and TG levels in *APOE2*.*Apoe*-/- mice. Despite the absence of the C-terminal lipid-binding domain, *APOE4*-202 is apparently capable of binding to lipoproteins and mediating hepatic uptake. Moreover, overexpression of *APOE4*-202 in *APOE2*.*Apoe*-/- mice does not aggravate their *hypertriglyceridemia*. These results extend our previous analyses of *APOE4*-202 expression in *Apoe*-/- mice and demonstrate that *apoE4*-202 functions even in the presence of clearance-defective *apoE2*. Thus, *apoE4*-202 is a safe and efficient candidate for future therapeutic applications.

; Adenoviridae--genetics--GE; Adenoviridae--metabolism--ME; Animals; Apolipoproteins E--chemistry--CH; *Cholesterol*--blood--BL; Hyperlipidemia --genetics--GE; Lipids--blood--BL; Lipoproteins--blood--BL; Lipoproteins, VLDL--chemistry--CH; Lipoproteins, VLDL--metabolism--ME; Liver--metabolism --ME; Mice; Mice, Transgenic...

Chemical Name: Apolipoproteins E; Lipids; Lipoproteins; Lipoproteins, VLDL; Protein Isoforms; Triglycerides; apolipoprotein E-2; apolipoprotein E-4; very low density lipoprotein triglyceride; *Cholesterol*

4/3,K/2 (Item 2 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

12492146 PMID: 12950448

Lipoproteins produced by ApoE-/- astrocytes infected with adenovirus expressing human ApoE.

Peng Dacheng; Song Ching; Reardon Catherine A; Liao Shutsung; Getz Godfrey S

Department of Pathology, University of Chicago, Chicago, Illinois, USA.

Journal of neurochemistry (England) Sep 2003, 86 (6) p1391-402, ISSN 0022-3042 Journal Code: 2985190R

Contract/Grant No.: DK42086; DK; NIDDK; NS520138; NS; NINDS

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

We have developed an astrocyte cell culture system that is attractive for

the study of *apoE* structure and its impact on astrocyte lipoproteins and neuronal function. Primary astrocytes from *apoE*-/- mice were infected with *adenovirus* expressing *apoE3* or *apoE4* and the nascent lipoproteins secreted were characterized. The nascent *apoE*-containing astrocyte particles were predominantly the size of plasma high density lipoprotein (HDL). *ApoE4*, in contrast to *apoE3* , appeared to be distributed in two distinct lipoprotein peaks and the *apoE4*-containing lipoproteins contained significantly more radiolabeled triglyceride. On electron micrographs the astrocyte particles were both discoidal and spherical in shape with a prevalence of stacked discs in *apoE3* particles, but single discs and larger spheres in *apoE4* particles. The *apoE4* discs were significantly wider than *apoE3* discs. These properties of the astrocyte lipoproteins are similar to those obtained from *apoE* isoform transgenic mice. Astrocyte lipoproteins containing *apoE3*, but not *apoE4* , stimulated neurite outgrowth in Neuro-2a cells. These studies suggest that the isoform-specific effects of *apoE* lipoproteins may involve differences in particle size and composition. Finally we demonstrate the usefulness of this system by expressing a *truncated* *apoE3* (delta202-299) mutant and show preliminary data indicating that a liver X receptor agonist promotes HDL output by the astrocytes without an increase in *apoE* in the media. This cell culture system is more flexible and allows for more rapid expression of *apoE* mutants.

...; deficiency--DF; Apolipoproteins E--ultrastructure--UL; Astrocytes --cytology--CY; Astrocytes--drug effects--DE; Astrocytes--virology--VI; Cell Differentiation--drug effects--DE; Cell Fractionation; Cells, Cultured ; *Cholesterol*--analysis--AN; *Cholesterol*--metabolism--ME; Cholic Acids --pharmacology--PD; Lipoproteins, HDL--chemistry--CH; Lipoproteins, HDL --pharmacology--PD; Mice; Microscopy, Electron; Neurons--cytology--CY; Neurons--drug effects--DE; Phospholipids...

Chemical Name: 3,6-dihydroxy-5-cholanoic acid-N-methyl-N-methoxy-24-amide ; Apolipoproteins E; Cholic Acids; Lipoproteins, HDL; Phospholipids; apolipoprotein E-3; apolipoprotein E-4; *Cholesterol*

4/3,K/3 (Item 3 from file: 155)

12480883 PMID: 12924933

Molecular mechanisms of type III hyperlipoproteinemia: The contribution of the carboxy-terminal domain of ApoE can account for the dyslipidemia that is associated with the E2/E2 phenotype.

Kypreos Kyriakos E; Li Xiaoping; van Dijk Ko Willems; Havekes Louis M; Zannis Vassilis I

Molecular Genetics, Department of Medicine, Boston University School of Medicine, Boston, Massachusetts 02118-2394, USA.

Biochemistry (United States) Aug 26 2003, 42 (33) p9841-53, ISSN 0006-2960 Journal Code: 0370623

Contract/Grant No.: HL68216; HL; NHLBI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

... has reduced affinity for the LDL receptor and is associated with type III hyperlipoproteinemia in humans. Consistent with these observations, we have found that following *adenovirus*-mediated gene transfer, full-length *apoE2* aggravates the hypercholesterolemia and induces *hypertriglyceridemia* in E-deficient mice and induces combined hyperlipidemia in C57BL/6 mice. Unexpectedly, the *truncated* *apoE2*-202 form that has an R158 for C substitution when expressed at levels similar to those of the full-length *apoE2* normalized the *cholesterol* levels of E-deficient mice without induction of *hypertriglyceridemia*. The *apoE2* truncation increased the affinity of POPC-*apoE* particles for the LDL receptor, and the full-length *apoE2* had a dominant effect in VLDL triglyceride secretion. Hyperlipidemia in normal C57BL/6 mice was prevented by coinfection with equal doses of each, the *apoE2* and the *apoE2*

-202-expressing adenoviruses, indicating that *truncated* *apoE* forms have a dominant effect in remnant clearance. *Hypertriglyceridemia* was completely corrected by coinfection of mice with an *adenovirus*-expressing wild-type lipoprotein lipase, whereas an inactive lipoprotein lipase had a smaller effect. The findings suggest that the *apoE2*-induced dyslipidemia is not merely the result of substitution of R158 for C but results from increased secretion of a triglyceride-enriched VLDL that cannot undergo lipolysis, inhibition of LpL activity, and impaired clearance of chylomicron remnants. Infection of E(-)(/)(-)xLDLr(-)(/)(-) double-deficient mice with *apoE2*-202 did not affect the plasma *cholesterol* levels, and also did not induce *hypertriglyceridemia*. In contrast, *apoE2* exacerbated the hypercholesterolemia and induced *hypertriglyceridemia*, suggesting that the LDL receptor is the predominant receptor in remnant clearance.

; Adenoviridae--genetics--GE; Animals; Apolipoproteins E--deficiency--DF; Apolipoproteins E--genetics--GE; Biological Transport, Active--genetics --GE; CHO Cells; *Cholesterol*--blood--BL; Genes, Dominant; Hamsters; Hyperlipidemia--pathology--PA; Hyperlipoproteinemia Type III--pathology--PA ; Lipolysis; Lipoprotein Lipase--genetics--GE; Lipoprotein Lipase --metabolism--ME; Lipoproteins, VLDL--secretion...

Chemical Name: Apolipoproteins E; Lipoproteins, VLDL; Phosphatidylcholines; Receptors, LDL; Triglycerides; apolipoprotein E-2; *Cholesterol*; 1-palmitoyl-2-oleoylphosphatidylcholine; Lipoprotein Lipase

4/3,K/4 (Item 4 from file: 155)

11303066 PMID: 11279066

Domains of apolipoprotein E contributing to triglyceride and *cholesterol* homeostasis in vivo. Carboxyl-terminal region 203-299 promotes hepatic very low density lipoprotein-triglyceride secretion.

Kypreos K E; van Dijk K W; van Der Zee A; Havekes L M; Zannis V I

Whitaker Cardiovascular Institute, Department of Medicine, Boston University School of Medicine, Boston, Massachusetts 02118, USA.

Journal of biological chemistry (United States) Jun 8 2001, 276 (23) p19778-86, ISSN 0021-9258 Journal Code: 2985121R

Contract/Grant No.: AG12717; AG; NIA

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Domains of apolipoprotein E contributing to triglyceride and *cholesterol* homeostasis in vivo. Carboxyl-terminal region 203-299 promotes hepatic very low density lipoprotein-triglyceride secretion.

Apolipoprotein (apo) E has been implicated in *cholesterol* and triglyceride homeostasis in humans. At physiological concentration *apoE* promotes efficient clearance of *apoE*-containing lipoprotein remnants. However, high *apoE* plasma levels correlate with high plasma triglyceride levels. We have used *adenovirus*-mediated gene transfer in *apoE* -deficient mice (E(-)/-) to define the domains of *apoE* required for *cholesterol* and triglyceride homeostasis in vivo. A dose of 2 x 10(9) plaque-forming units of *apoE4*-expressing *adenovirus* reduced slightly the *cholesterol* levels of E(-)/- mice and resulted in severe *hypertriglyceridemia*, due to accumulation of *cholesterol* and triglyceride-rich very low density lipoprotein particles in plasma. In contrast, the *truncated* form *apoE4*-202 resulted in a 90% reduction in the plasma *cholesterol* levels but did not alter plasma triglyceride levels in the E(-)/- mice. *ApoE* secretion by cell cultures, as well as the steady-state hepatic mRNA levels in individual mice expressing *apoE4* or *apoE4* -202, were similar. In contrast, very low density lipoprotein-triglyceride secretion in mice expressing *apoE4*, but not *apoE4* -202, was increased 10-fold, as compared with mice infected with a control *adenovirus* . The findings suggest that the amino-terminal 1-202 region of *apoE4* contains the domains required for the in vivo clearance

of lipoprotein remnants. Furthermore, the carboxyl-terminal 203-299 residues of *apoE* promote hepatic very low density lipoprotein-triglyceride secretion and contribute to *apoE*-induced *hypertriglyceridemia*.

Descriptors: Apolipoproteins E--metabolism--ME; **Cholesterol* --metabolism--ME; *Homeostasis; *Triglycerides--metabolism--ME; Adenovirida e--genetics--GE; Animals; Apolipoproteins E--blood--BL; Apolipoproteins E --chemistry--CH; Apolipoproteins E--genetics--GE; Base Sequence; *Cholesterol*--blood--BL; Chromatography, Liquid; DNA Primers; Liver --metabolism--ME; Mice; Mice, Knockout; RNA, Messenger--genetics--GE; RNA, Messenger--metabolism--ME; Triglycerides--blood--BL; Tumor Cells...

Chemical Name: Apolipoproteins E; DNA Primers; RNA, Messenger; Triglycerides; apolipoprotein E-4; *Cholesterol*

4/3,K/5 (Item 5 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

11274308 PMID: 11352738

The amino-terminal 1-185 domain of apoE promotes the clearance of lipoprotein remnants in vivo. The carboxy-terminal domain is required for induction of hyperlipidemia in normal and apoE-deficient mice.

Kypreos K E; Morani P; van Dijk K W; Havekes L M; Zannis V I

Whitaker Cardiovascular Institute, Department of Medicine, Boston University School of Medicine, Boston, Massachusetts 02118-2394, USA.

Biochemistry (United States) May 22 2001, 40 (20) p6027-35, ISSN 0006-2960 Journal Code: 0370623

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Apolipoprotein E (*apoE*) promotes receptor-mediated catabolism of *apoE* -containing lipoprotein remnants. Impairments in remnant clearance are associated with type III hyperlipoproteinemia and premature atherosclerosis. In humans, *apoE* plasma levels correlate with plasma triglyceride levels, suggesting that excess *apoE* may also affect plasma triglyceride levels. We have used *adenovirus*-mediated gene transfer in mice to map the domains of *apoE* required for *cholesterol* and triglyceride clearance, in vivo. *Adenovirus* expressing *apoE3* and *apoE4* at doses of (1-2) x 10(9) pfu increased plasma *cholesterol* and triglyceride levels in normal C57BL6 mice and failed to normalize the high *cholesterol* levels of *apoE*-deficient mice due to induction of *hypertriglyceridemia*. In contrast, an *adenovirus* expressing the *truncated* *apoE* 1-185 form normalized the *cholesterol* levels of E(-)(/)(-) mice and did not cause *hypertriglyceridemia*. Northern blot analysis of hepatic RNA from mice expressing the full-length and the *truncated* *apoE* forms showed comparable steady-state *apoE* mRNA levels of the full-length *apoE* forms that cause hyperlipidemia and the *truncated* *apoE* forms that do not cause hyperlipidemia. The findings suggest that the amino-terminal residues 1-185 of *apoE* are sufficient for the clearance of *apoE* -containing lipoprotein remnants by the liver, whereas domains of the carboxy-terminal one-third of *apoE* are required for *apoE*-induced hyperlipidemia.

Descriptors: ...; Gene Deletion; Genetic Vectors--chemistry--CH; Genetic Vectors --metabolism--ME; Hypercholesterolemia--blood--BL; Hypercholesterolemia --etiology--ET; Hypercholesterolemia--genetics--GE; Hyperlipidemia--blood --BL; Hyperlipidemia--etiology--ET; *Hypertriglyceridemia*--blood--BL; *Hypertriglyceridemia*--etiology--ET; *Hypertriglyceridemia*--genetics--GE ; Lipoproteins--blood--BL; Lipoproteins, VLDL--secretion--SE; Liver --secretion--SE; Mice; Mice, Inbred C57BL; Mice, Knockout; Peptide Fragments--genetics--GE; Protein Structure, Tertiary...

4/3,K/6 (Item 6 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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10292763 PMID: 7989859

Expression of heterologous human apolipoprotein E by J774 macrophages enhances *cholesterol* efflux to HDL3.

Mazzone T; Reardon C

Department of Medicine, Rush Medical College, Chicago, IL 60612.

Journal of lipid research (UNITED STATES) Aug 1994, 35 (8) p1345-53, ISSN 0022-2275 Journal Code: 0376606

Contract/Grant No.: HL15062; HL; NHLBI; HL39653; HL; NHLBI

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Expression of heterologous human apolipoprotein E by J774 macrophages enhances *cholesterol* efflux to HDL3.

Expression of apolipoprotein (apo) E by macrophages is tightly regulated by cellular *cholesterol* content. We have investigated a potential modulating role for *apoE* on macrophage *cholesterol* homeostasis by stably transfecting the J774 macrophage, which does not express its endogenous *apoE* gene, with a human *apoE* cDNA expression *vector* and comparing *cholesterol* homeostasis in this cell line with that of a control line transfected with the neomycin resistance construct only. Incubation in serum-free medium after *cholesterol* loading produced no difference in cellular *cholesterol* content between *apoE* secreting and non-secreting J774 cells. Similarly, in serum-free medium there was no difference in the amount of radiolabeled *cholesterol* effluxed. Addition of cAMP or S58035 to *cholesterol*-loaded J774 cells did enhance efflux of radiolabeled *cholesterol* from *apoE* secreting compared to non-secreting macrophages but did not detectably alter cellular free *cholesterol* or cholesteryl ester mass. Incubation with HDL3 alone, however, significantly decreased macrophage cholesteryl ester mass compared to a 24-h incubation in serum-free medium from 10.5 +/- 3.9 to 3.2 +/- 2.0 (P < 0.01) in *apoE* -secreting J774 cells. During a 24-h incubation in HDL3, cholesteryl ester fell from 6.4 +/- 2.4 to 0.8 +/- 0.7 (delta = 5.6 micrograms/mg) in *apoE* -secreting cells and from 9.3 +/- 2.2 to 7.7 +/- micrograms/mg (delta = 1.6 micrograms/mg) in non-secreting cells (P < 0.005 *apoE*-secreting vs. non-secreting cells).(ABSTRACT *TRUNCATED* AT 250 WORDS)

Descriptors: Apolipoproteins E--secretion--SE; **Cholesterol*--metabolism --ME; *Lipoproteins, HDL--pharmacology--PD; *Macrophages--metabolism--ME; Apolipoproteins E--genetics--GE; Cell Line; *Cholesterol*--pharmacology--PD ; *Cholesterol* Esters--metabolism--ME; DNA, Complementary; Gene Transfer Techniques; Macrophages--drug effects--DE

Chemical Name: Apolipoproteins E; *Cholesterol* Esters; DNA, Complementary; Lipoproteins, HDL; *Cholesterol*

```
?ds

Set     Items   Description
S1        253   (TRUNCATED) (S) (APOE3 OR APOE-3 OR APOE?)
S2         22   S1 (S) (VECTOR OR PLASMID OR ADENOVIRUS OR ADENOVIRAL)
S3         14   S2 AND (CHOLESTEROL OR HYPERTRIGLYCERIDEMIA)
S4          6   RD (unique items)
?s s2 not s3
              22  S2
              14  S3
      S5       8  S2 NOT S3
?rd
...completed examining records
      S6       5  RD (unique items)
?t s6/3,k/all
```

6/3,K/1 (Item 1 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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13506211 PMID: 9192073

Bacterial overexpression, isotope enrichment, and NMR analysis of the N-terminal domain of human apolipoprotein E.

Fisher C A; Wang J; Francis G A; Sykes B D; Kay C M; Ryan R O
Lipid and Lipoprotein Research Group, University of Alberta, Edmonton, Canada.

Biochemistry and cell biology = Biochimie et biologie cellulaire (CANADA) 1997, 75 (1) p45-53, ISSN 0829-8211 Journal Code: 8606068
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The nucleotide sequence encoding the N-terminal domain (residues 1-183) of human apolipoprotein E3 (*apoE3*) was cloned into the pET expression *vector* and introduced into Escherichia coli. Induction of protein expression with isopropyl beta-D-thiogalactopyranoside resulted in production of recombinant *apoE3*(1-183). Immunoblot analysis revealed that recombinant protein was present in both the cell pellet and cell culture supernatant. Analysis revealed that a significant portion of the rApoE3(1-183) in the cell pellet still possessed the bacterial N-terminal pel B leader sequence, encoded by *plasmid* DNA directly upstream of the *apoE3* (1-183) coding sequence. By contrast, this hydrophobic leader sequence had been removed from recombinant protein specifically accumulating in the culture medium. This behavior is novel for bacterial expression of apolipoprotein E and its *truncated* variants and permits efficient overexpression of the recombinant protein (> 100 mg/L cell culture). Recombinant *apoE3* (1-183) was isolated by a combination of heparin-Sepharose chromatography and reverse-phase HPLC. Electrospray mass spectrometry provided a mass of 21 191 daltons...

... helical secondary structure. The lipid binding ability of rApoE3(1-183) was evaluated using an in vitro lipoprotein binding assay. It was observed that recombinant *apoE3* (1-183) protected human low density lipoprotein (LDL) from lipid accumulation induced particle aggregation, indicating that it is capable of associating with lipoprotein surfaces. In...

... the apoB/E receptor on human skin fibroblasts to an extent similar to that observed for intact rApoE3. Taken together, these data show that recombinant *apoE3* (1-183) is fully functional as an apolipoprotein and receptor ligand. Given the high expression level and its known existence as a monomer in solution...
... study the structure-function relationship of rApoE3(1-183). Bacteria were cultured in media supplemented with 15NH4Cl or [15N]glycine and the isotopically labeled recombinant *apoE3* (1-183) was analyzed by heteronuclear single quantum correlation NMR spectroscopy. The data revealed that rApoE3(1-183) is an excellent candidate for solution structure...

6/3,K/2 (Item 2 from file: 155)

08248484 PMID: 2475506

Apolipoprotein B48 RNA editing in chimeric apolipoprotein EB mRNA.

Bostrom K; Lauer S J; Poksay K S; Garcia Z; Taylor J M; Innerarity T L
Department of Physiology, Gladstone Foundation Laboratory for Cardiovascular Disease, University of California, San Francisco 94140-0608.

Journal of biological chemistry (UNITED STATES) Sep 15 1989, 264 (26) p15701-8, ISSN 0021-9258 Journal Code: 2985121R
Contract/Grant No.: HL41633; HL; NHLBI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

... apoB mRNA editing mechanism, two apoB cDNA fragments (354 and 63 base

pairs) with codon 2153 near their centers were inserted into a high expression *vector* of another secreted apolipoprotein, *apoE* . The resulting vectors, pHEB-354 and -63, were transfected into Chinese hamster ovary cells, HepG2 cells, and apoB48-producing CaCo-2 cells. The secreted chimeric apolipoproteins (*apoEB354* and *apoEB63*) were analyzed for premature truncation, and the mRNA was analyzed for the presence of an edited base. The pHEB-354 construct produced a *truncated* protein only in CaCo-2 cells, whereas pHEB-63 produced no *truncated* protein in any of the three cell types. The mRNA was converted to cDNA and amplified by the polymerase chain reaction technique. Differential hybridization of...

6/3,K/3 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014537216 BIOSIS NO.: 200300494873
Lipoproteins produced by ApoE-/- astrocytes infected with adenovirus expressing human ApoE.
AUTHOR: Peng Dacheng; Song Ching; Reardon Catherine A; Liao Shutsung; Getz Godfrey S (Reprint)
AUTHOR ADDRESS: Department of Pathology, University of Chicago, 5841 S. Maryland Ave, MC 1089, Chicago, IL, 60637-1470, USA**USA
AUTHOR E-MAIL ADDRESS: g-getz@uchicago.edu
JOURNAL: Journal of Neurochemistry 86 (6): p1391-1402 September 2003 2003
MEDIUM: print
ISSN: 0022-3042
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We have developed an astrocyte cell culture system that is attractive for the study of *apoE* structure and its impact on astrocyte lipoproteins and neuronal function. Primary astrocytes from *apoE*-/- mice were infected with *adenovirus* expressing *apoE3* or *apoE4* and the nascent lipoproteins secreted were characterized. The nascent *apoE* -containing astrocyte particles were predominantly the size of plasma high density lipoprotein (HDL). *ApoE4*, in contrast to *apoE3*, appeared to be distributed in two distinct lipoprotein peaks and the *apoE4* -containing lipoproteins contained significantly more radiolabeled triglyceride. On electron micrographs the astrocyte particles were both discoidal and spherical in shape with a prevalence of stacked discs in *apoE3* particles, but single discs and larger spheres in *apoE4* particles. The *apoE4* discs were significantly wider than *apoE3* discs. These properties of the astrocyte lipoproteins are similar to those obtained from *apoE* isoform transgenic mice. Astrocyte lipoproteins containing *apoE3*, but not *apoE4*, stimulated neurite outgrowth in Neuro-2a cells. These studies suggest that the isoform-specific effects of *apoE* lipoproteins may involve differences in particle size and composition. Finally we demonstrate the usefulness of this system by expressing a *truncated* *apoE3* (DELTA202-299) mutant and show preliminary data indicating that a liver X receptor agonist promotes HDL output by the astrocytes without an increase in *apoE* in the media. This cell culture system is more flexible and allows for more rapid expression of *apoE* mutants.

6/3,K/4 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014410315 BIOSIS NO.: 200300369034
Inhibitory Antibody Formation Against Factor VIII Derived from Different Species after Naked DNA Transfer into Hemophilia A Mice.
AUTHOR: Ye Peiqing (Reprint); Thompson Arthur R; Sarkar Rita; Kazazian Haig H; Lillicrap David P (Reprint); Kaufman Randal J; Ochs Hans D; Rawlings David J; Miao Carol H

AUTHOR ADDRESS: Depts. of Pediatrics and Medicine, University of Washington, Puget Sound Blood Center, Seattle, WA, USA**USA
JOURNAL: Blood 100 (11): pAbstract No. 5550 November 16, 2002 2002
MEDIUM: print
CONFERENCE/MEETING: 44th Annual Meeting of the American Society of Hematology Philadelphia, PA, USA December 06-10, 2002; 20021206
SPONSOR: American Society of Hematology
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Poster; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

...ABSTRACT: therapy protocols may stimulate additional or different immune responses as compared to repeated infusion of proteins. Recently, we have developed a high-expressing, liver-specific *vector*, pBS-HCRHPI-A, containing a hepatic locus control region from *ApoE* gene (HCR), alpha1-antitrypsin promoter (HP), a *truncated* human factor IX (hFIX) intron (I), a multiple cloning site to accommodate heterologous cDNA, and a bovine growth hormone polyadenylation signal (A). Three B-domain deleted factor VIII cDNAs derived from human, canine, and murine origins were each inserted into the multiple cloning site of the *vector* to yield pBS-HCRHPI-FVIIIA, pBS-HCRHPI-cFVIIIA, pBS-HCRHPI-mFVIIIA. Fifty mug of the *plasmid* in 2 ml solution was rapidly injected into the tail vein of three groups of hemophilia A mice (n=6/each group). Factor VIII levels...

...fell gradually to undetectable levels within 2-3 weeks. This correlated with the presence of inhibitory antibody formation. Southern analysis of genomic DNA isolated from *plasmid*-treated mice showed that FVIII *plasmid* DNA persistently maintained in the liver. Western blotting of FVIII protein demonstrated that all the treated mice persistently expressed FVIII protein despite of the reduction...

...canine, and murine FVIII cDNA, supporting the conclusion that these antibody responses were unrelated to species differences. Since there was no immune response towards the *plasmid* DNA in the liver, FVIII *plasmid* treated-hemophilia A mice represent an excellent model system for study of inhibitory antibody formation. This response is specific to persistent FVIII expression and independent...

6/3,K/5 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013593413 BIOSIS NO.: 200200186924
High-level gene expression of human factor VIII in vivo was achieved by a liver-specific construct containing ApoE-HCR and a heterologous intron
AUTHOR: Miao Carol H (Reprint); Ye Xin (Reprint); Thompson Arthur R (Reprint)
AUTHOR ADDRESS: Medicine, Puget Sound Blood Center, University of Washington, Seattle, WA, USA**USA
JOURNAL: Blood 98 (11 Part 1): p425a November 16, 2001 2001
MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001; 20011207
SPONSOR: American Society of Hematology
ISSN: 0006-4971
DOCUMENT TYPE: Meeting; Meeting Abstract; Meeting Poster
RECORD TYPE: Abstract
LANGUAGE: English

...ABSTRACT: developed two nonviral gene transfer vectors for high-level gene expression in the liver. The expression cassettes contain 1) a hepatic locus control region from *ApoE* gene (*ApoE*-HCR), 2) a liver-specific alpha1-antitrypsin promoter (HP), 3) a 1.4kb *truncated* factor IX intron (I) or a synthetic minx intron (mI), followed by 4) a

multiple cloning site for inserting cDNA sequences, and 5) a bovine...

...25.5 mug/ml and 0.7-5 mug/ml of human factor VIII circulated, respectively (normal=0.1mug/ml in human plasma). A control *plasmid*, pBS-HP-FVIIIA, without the *ApoE*-HCR or an intronic sequence, produced levels less than 0.05 mug/ml. These results are in parallel with those obtained from the high expressing human factor IX *plasmid*, pBS-HCRHP-FIXIA, where the *truncated* first intron of factor IX was in its native position between exons 1 and 2 (Miao et al. (2001) Mol. Ther. 3, 947-57). Our data demonstrate that combination of *ApoE*-HCR and a heterologous intron, either a *truncated* human factor IX first intron or a synthetic minx intron inserted 5' to factor VIII cDNA can greatly enhance factor VIII gene expression in vivo...

...of interest to investigate whether the expression can be further enhanced by inserting a heterologous intron or factor VIII introns into different positions in the *vector*. Furthermore, the liver-specific vectors can be used to deliver heterologous genes for high-level transgene expression. These high-expressing human factor VIII cassettes can...

```
?ds     '

Set     Items   Description
S1        253   (TRUNCATED) (S) (APOE3 OR APOE-3 OR APOE?)
S2         22   S1 (S) (VECTOR OR PLASMID OR ADENOVIRUS OR ADENOVIRAL)
S3         14   S2 AND (CHOLESTEROL OR HYPERTRIGLYCERIDEMIA)
S4          6   RD (unique items)
S5          8   S2 NOT S3
S6          5   RD (unique items)
?s s1 and (treatment or therapy)
             253  S1
         4363788  TREATMENT
         4970712  THERAPY
      S7      23  S1 AND (TREATMENT OR THERAPY)
?rd
...completed examining records
      S8      20  RD (unique items)
?s s8 not s2
             20  S8
             22  S2
      S9      18  S8 NOT S2
?t s9/3,k/all
```

9/3,K/1 (Item 1 from file: 155)

DIALOG(R)File 155:MEDLINE(R)
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15108176 PMID: 14503965

High-level factor VIII gene expression in vivo achieved by nonviral liver-specific gene *therapy* vectors.

Miao Carol H; Ye Xin; Thompson Arthur R
Department of Pediatrics and Medicine, University of Washington, WA 98195, USA. miao@u.washington.edu

Human gene therapy (United States) Sep 20 2003, 14 (14) p1297-305, ISSN 1043-0342 Journal Code: 9008950
Contract/Grant No.: 2P30DK47754-08; DK; NIDDK
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process

High-level factor VIII gene expression in vivo achieved by nonviral liver-specific gene *therapy* vectors.

... nonviral gene transfer vectors have been developed to accommodate heterologous genes. The expression cassettes contain (1) a hepatic locus control region from the apolipoprotein E (*ApoE*) gene (HCR), (2) a liver-specific alpha(1)-antitrypsin promoter (HP), (3) a 1.4-kb *truncated*

factor IX first intron (I) or a synthetic minx intron (mI), (4) a multiple cloning site (MCS) for inserting cDNA sequences, and (5) a bovine...

... initially in both C57BL/6 mice and Rag2 mice. Moreover, therapeutic levels of hFVIII (20-310 ng/ml) circulated in Rag2 mice 6 months after *treatment* . These liver-specific gene expression cassettes can deliver a large, heterologous gene such as hFVIII cDNA to achieve high-level, persistent transgene expression after in vivo hepatic gene *therapy*.

9/3,K/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12847880 PMID: 7489235

Effects of 1 year of growth hormone *therapy* on serum lipoprotein levels in growth hormone-deficient adults. Influence of gender and Apo(a) and ApoE phenotypes.

Johannsson G; Oscarsson J; Rosen T; Wiklund O; Olsson G; Wilhelmsen L; Bengtsson B A
Research Centre for Endocrinology and Metabolism, Sahlgrenska University Hospital, Goteborg, Sweden.

Arteriosclerosis, thrombosis, and vascular biology (UNITED STATES) Dec 1995, 15 (12) p2142-50, ISSN 1079-5642 Journal Code: 9505803
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Effects of 1 year of growth hormone *therapy* on serum lipoprotein levels in growth hormone-deficient adults. Influence of gender and Apo(a) and ApoE phenotypes.

We investigated the influence of gender and *apoE* and apo(a) phenotypes as well as the effect of the metabolic effects of growth hormone (GH) on the effect of GH *therapy* on serum lipoprotein concentrations in GH-deficient (GHD) adults. Forty-four consecutive patients, 30 men and 14 women aged 46.5 (range, 19 to 76...

... Serum concentrations of lipoproteins, insulin, thyroxine, and insulin-like growth factor-I were determined, body composition was assessed by bioelectrical impedance, and apo(a) and *apoE* phenotypes were analyzed. Lipoprotein(a) [Lp(a)] concentrations in the GHD subjects were compared with a gender- and apo(a) phenotype-matched control group. After 12 months of GH *treatment* , the total cholesterol, LDL cholesterol, and apoB concentrations decreased, the HDL cholesterol and *apoE* concentrations increased, and the apoA-I and triglyceride concentrations were unchanged. Before *treatment* , the Lp(a) concentration was similar to that in the control group. However, after 12 months of *treatment* , the Lp(a) concentration had increased by 44% and 101% above baseline and the control group, respectively. Men and women responded differently to GH, with...

...free mass and a more pronounced decrease in body-fat mass in men. Apo(a) phenotypes had no major influence on the effect of GH *therapy*. The only significant difference between *apoE* phenotypes was a higher baseline Lp(a) concentration among *apoE4* heterozygotes.(ABSTRACT *TRUNCATED* AT 250 WORDS)

9/3,K/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

12744462 PMID: 7666000

In vivo cholesterol kinetics in apolipoprotein E-deficient and control mice.

Quarfordt S H; Oswald B; Landis B; Xu H S; Zhang S H; Maeda N
Department of Medicine, Durham VA Hospital, NC 27705, USA.

Journal of lipid research (UNITED STATES) Jun 1995, 36 (6) p1227-35, ISSN 0022-2275 Journal Code: 0376606
Contract/Grant No.: HL-42630; HL; NHLBI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The in vivo total body cholesterol transport of homozygous *apoE* -deficient (-/-) and control (+/+) mice was evaluated by compartmental analysis of plasma cholesterol decay. Body cholesterol fractional catabolic rates of chow fed mutants were less (-/-, 0...

... with impaired hepatic uptake of cholesterol, mutants had much slower plasma clearance of lipoprotein cholesterol, as well as slower transfer to catabolic pools than normals. *Treatment* of homozygotes with lovastatin doubled both plasma cholesterol concentration and body cholesterol transport indicating the importance of *apoE*-dependent cell cholesterol transfer in synthetic down-regulation with this agent. These data indicate that mice lacking *apoE* have lower affinity hepatic uptake of plasma remnant cholesterol.(ABSTRACT *TRUNCATED* AT 250 WORDS)

9/3,K/4 (Item 4 from file: 155)

12662974 PMID: 7787776
Thiamine homeostasis in neuroblastoma cells.
Bettendorff L
Laboratory of Neurochemistry, University of Liege, Belgium.
Neurochemistry international (ENGLAND) Mar 1995, 26 (3) p295-302, ISSN 0197-0186 Journal Code: 8006959
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

... by Ca2+. The driving force for thiamine uptake is its phosphorylation to thiamine diphosphate (TDP) by thiamine pyrophosphokinase and subsequent binding of this cofactor to *apoenzymes*. Our results suggest that cells of neuronal origin possess mechanisms regulating the intracellular concentration of thiamine. At low external thiamine, the vitamin is taken up...

... thiamine is observed at low external concentration of the vitamin. At higher external thiamine concentration, TDP accumulation is limited by the binding capacity to the *apoenzymes* and unbound TDP (i.e. a small pool of fast turnover) is quickly hydrolyzed. Thiamine is slowly released by the cells by at least two...

... thiamine efflux is neither sensitive to veratridine nor to Ca2+ and its mechanism is unknown. About 25% of intracellular thiamine is not released, even after *treatment* of the cells with digitonin, thus maintaining an apparent gradient. This suggests a binding or sequestration in intracellular compartments.(ABSTRACT *TRUNCATED* AT 250 WORDS)

9/3,K/5 (Item 5 from file: 155)

10283173 PMID: 7981178
Effects of lovastatin on ApoA- and ApoB-containing lipoproteins. Families in a subpopulation of patients participating in the Monitored Atherosclerosis Regression Study (MARS).
Alaupovic P; Hodis H N; Knight-Gibson C; Mack W J; LaBree L;

Cashin-Hemphill L; Corder C N; Kramsch D M; Blankenhorn D H
Lipid and Lipoprotein Laboratory, Oklahoma Medical Research Foundation, Oklahoma City 73104.
Arteriosclerosis and thrombosis - a journal of vascular biology / American Heart Association (UNITED STATES) Dec 1994, 14 (12) p1906-13, ISSN 1049-8834 Journal Code: 9101388
Contract/Grant No.: HL-45005; HL; NHLBI; HL-49885; HL; NHLBI
Document type: Clinical Trial; Journal Article; Randomized Controlled Trial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

... cholesterol intake of less than 250 mg. The plasma lipid and apolipoprotein profiles were determined at the time of randomization and after 2 years of *treatment*, and the levels of apoA- and apoB-containing lipoprotein families were measured after 2 years of *treatment*. After this *treatment* period, the drug group was characterized in comparison with the placebo group by significantly reduced levels of total cholesterol (33%), triglycerides (30%), very-low-density lipoprotein cholesterol (36%), low-density lipoprotein cholesterol (43%), apoB (36%), apoC-III (18%), and *apoE* (17%) and slightly but insignificantly increased levels of high-density lipoprotein cholesterol (6%) and apoA-I (1%). The 2-year levels of lipoprotein containing apoA...

... I and apoA-II (LpA-I/A-II) particles separated by immunoaffinity chromatography on an anti-apoA-II immunosorber did not differ between the two *treatment* groups. However, the apoB-containing lipoprotein (Lp) families defined by apolipoprotein composition and separated by immunoaffinity chromatography on anti-apoA-II and anti-apoC-III immunosorbers were affected in a selective manner.(ABSTRACT *TRUNCATED* AT 250 WORDS)
; Adult; Aged; Cholesterol--blood--BL; Coronary Arteriosclerosis--drug *therapy*--DT; Disease Progression; Drug Monitoring; Hypercholesterolemia --drug *therapy*--DT; Lovastatin--therapeutic use--TU; Middle Aged; Triglycerides--blood--BL

9/3,K/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10282779 PMID: 7980718
Triglyceride-rich lipoproteins of subjects heterozygous for apolipoprotein E2(Lys146-->Gln) are inefficiently converted to cholesterol-rich lipoproteins.
Mulder M; van der Boom H; de Knijff P; Braam C; van den Maagdenberg A; Leuven J A; Havekes L M
TNO Institute of Prevention and Health Research, Gaubius Laboratory, Leiden, The Netherlands.
Atherosclerosis (IRELAND) Aug 1994, 108 (2) p183-92, ISSN 0021-9150 Journal Code: 0242543
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

The *APOE* *2(Lys146-->Gln) allele behaves like a dominant trait in the expression of familial dysbetalipoproteinemia (FD) (Smit et al., J. Lipid Res. 1990; 31: 45-53). FD patients carrying the *APOE**2(Lys146-->Gln) allele exhibit less elevated cholesterol to triglyceride ratios in the d < 1.019 g/ml lipoprotein density fraction as compared to classical FD patients displaying homozygosity for the *APOE**2(Arg158-->Cys) allele (0.8 vs. 1.4). Upon *treatment* of complete serum with lipoprotein lipase (LPL), the mean cholesterol to triglyceride molar ratio of the d < 1.019 g/ml lipoprotein fraction in these...

... 0.7 to 1.5). In order to obtain further evidence for an inefficient lipolysis of the d < 1.019 g/ml lipoprotein fraction in *APOE* *2(Lys146-->Gln) carriers, possibly in combination with a less efficient cholesteryl ester transfer protein (CETP) activity, blood samples of *APOE* *2(Lys146-->Gln) allele carrying FD patients were analysed and compared with classical FD patients and controls. In the *APOE**2(Lys149-->Gln) allele carrying FD patients were analysed and compared with classical FD patients and controls. In the *APOE* *2(Lys146-->Gln) FD patients, the increase in plasma cholesterol was mainly confined to the very low density lipoprotein (VLDL) fraction, whereas in classical FD...

... density lipoprotein (IDL) fraction was also dramatically increased (ratios of VLDL to IDL cholesterol are 4.7 and 2.6, respectively). Family analyses of the *APOE**2(Lys146-->Gln) FD subjects showed that the apo E to apo B ratio in the d < 1.019 g/ml lipoprotein fraction of allele carriers is 3.5 times as high as that found in non-carriers (2.8 vs. 0.8, by wt.). Also, in the *APOE* *2(Lys146-->Gln) allele carrying family members, the ratio of cholesterol to triglyceride of the d < 1.019 g/ml lipoprotein fraction is less markedly...

... controls (from 1.1 to 1.8 vs 0.7 to 1.6). The efficiency of the d < 1.019 g/ml lipoprotein fraction of *APOE**2(Lys146-->Gln) FD patients to compete with low density lipoprotein (LDL) for binding to the LDL receptor is intermediate to that of controls and classical *APOE**2(Arg158-->Cys) homozygous FD patients. These findings suggest that in *APOE* *2(Lys146-->Gln) allele carriers, the conversion of VLDL into IDL is impaired due to an inefficient lipolysis, possibly in combination with a retarded CETP activity.(ABSTRACT *TRUNCATED* AT 250 WORDS)

9/3,K/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10250173 PMID: 7951334
T-DNA-insert-independent mutations induced in transformed plant cells during Agrobacterium co-cultivation.
Marton L; Hrouda M; Pecsvaradi A; Czako M
Department of Biological Sciences, University of South Carolina, Columbia 29208.
Transgenic research (ENGLAND) Sep 1994, 3 (5) p317-25, ISSN 0962-8819 Journal Code: 9209120
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

... in Agrobacterium-mediated gene transfer experiments. An unexpected large drop (50%) in plating efficiencies was observed in the non-selected (control) 1n populations after transformation *treatment* with virulent strains. This effect was not observed in the 2n or 4n cultures or in the 1n cultures when treated with avirulent bacteria. The...

... Nicotiana plumbaginifolia protoplasts, as well as from leaf disc cultures or protoplasts of diploid plants that were heterozygotic for a mutation either in the NR *apoenzyme* gene (nia/wt) or one of the molybdenum-containing cofactor genes (cnxA/wt), after Agrobacterium co-cultivation. The chlorate-resistant isolates were tested for the...

... sequences in the mutated NR genes, despite the fact that NR-deficient cells were found more frequently in cell populations which became transformed during the *treatment* than in the populations which did not.(ABSTRACT *TRUNCATED* AT 250 WORDS)

9/3,K/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09029242 PMID: 1892811

Opposite facial specificity for two hydroquinone epoxidases: (3-si,4-re)-2,5-dihydroxyacetanilide epoxidase from Streptomyces LL-C10037 and (3-re,4-si)-2,5-dihydroxyacetanilide epoxidase from Streptomyces MPP 3051.

Shen B; Gould S J
Department of Chemistry, Oregon State University, Corvallis 97331-4003.

Biochemistry (UNITED STATES) Sep 17 1991, 30 (37) p8936-44, ISSN 0006-2960 Journal Code: 0370623
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

... at 0.04 mM), Ni2+ (relative V = 266 at 0.2 mM), or Co2+ (relative = 498 at 0.2 mM). Reconstitution from a DHAE I *apoenzyme*, generated by *treatment* with 1,10-phenanthroline followed by Sephadex G-25 chromatography, occurred only by addition of one of these three metals.(ABSTRACT *TRUNCATED* AT 250 WORDS)

9/3,K/9 (Item 9 from file: 155)

08291227 PMID: 2477479

Synthesis and secretion of apoE in thioglycolate-elicited mouse peritoneal macrophages: effect of cholesterol efflux.

Dory L
Department of Pharmacology, College of Medicine, University of Tennessee, Memphis 38163.

Journal of lipid research (UNITED STATES) Jun 1989, 30 (6) p809-16, ISSN 0022-2275 Journal Code: 0376606
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

ApoE synthesis and secretion, as a function of cellular cholesterol content and cholesterol efflux, was studied in thioglycolate-elicited mouse peritoneal macrophages. As expected, loading elicited macrophages with cholesterol induced a 5-fold increase in *apoE* secretion and a 2.5-fold increase in cellular *apoE* content over a 5-h period. *Treatment* of cholesterol-loaded cells with HDL3 further increased *apoE* secretion 1.7-fold and decreased cellular cholesterol by 20%. *Treatment* of cholesterol-loaded cells with HDL3 and SAH 58.035 (an ACAT inhibitor) increased *apoE* secretion 2.4-fold and decreased cellular cholesterol content by 35%. *Treatment* of the cells with the ACAT inhibitor alone suppressed *apoE* secretion by 40% but did not change cellular cholesterol content. Northern blot analysis of RNA indicated that cholesterol loading increased *apoE* mRNA 2-fold. *ApoE* mRNA levels were not further affected by *treatment* with HDL3 and/or the ACAT inhibitor. Cholesterol-loaded cells, in the absence of HDL3, secreted *apoE* into the media in two fractions as determined by column chromatography: a large molecular weight complex, (larger than HDL), and an essentially lipid-free protein. In the presence of HDL3, the cells secreted *apoE* in three fractions: a large molecular weight complex, an essentially lipid-free protein, and over 50% of *apoE* associated with HDL. In the process, HDL3 became larger and eluted in a position identical to that of HDL2. A small amount of HDL3-derived...

... LDL-size particle. Incubation of HDL3 in the absence of cholesterol-loaded cells did not produce these changes. It is concluded that cholesterol-loading increases *apoE* mRNA content and *apoE* synthesis.(ABSTRACT *TRUNCATED* AT 250 WORDS)

9/3,K/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08232823 PMID: 2761411
Serum lipids and apolipoproteins in the rat refed after starving: influence of the molecular form of nitrogen (protein, peptides, or free amino acids).
Poullain M G; Vacher D; Cezard J P; Girard-Globa A
Faculte de Medicine Xavier Bichat, Paris, France.
Metabolism- clinical and experimental (UNITED STATES) Aug 1989, 38 (8) p740-4, ISSN 0026-0495 Journal Code: 0375267
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Efficient *treatment* of deep denutrition should promote the restoration of normal intestinal villous structure and the return to a positive nitrogen balance. To determine whether the plasma...

... Starvation lowered the concentration of triglycerides and phospholipids but not cholesterol. Apolipoprotein AI and AIV concentrations were also significantly lowered (30% and 40%, respectively), but *ApoE* was significantly increased by 40%. Upon refeeding with all three diets, plasma lipids progressively returned to control values except for triglycerides, which were significantly elevated...

... mucosa; after 48 hours of refeeding, plasma concentrations of apo AIV were significantly correlated with jejunal villous height and protein content (P less than .01). *ApoE* was depressed below control levels in the WP and WPH groups at 24 and 48 hours and restored only after 96 hours. Because *ApoE* was affected, both in the fed state and during refeeding by the form of dietary nitrogen, it may prove to reflect nitrogen balance and/or insulin: glucagon balance.(ABSTRACT *TRUNCATED* AT 250 WORDS)

9/3,K/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08229649 PMID: 2503512
Topography of prostaglandin H synthase. Antiinflammatory agents and the protease-sensitive arginine 253 region.
Kulmacz R J
Department of Biological Chemistry, University of Illinois, Chicago 60612.
Journal of biological chemistry (UNITED STATES) Aug 25 1989, 264 (24) p14136-44, ISSN 0021-9258 Journal Code: 2985121R
Contract/Grant No.: GM 30509; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

... of indomethacin and similar agents on the protease sensitivity of the two enzymatic activities and of the synthase polypeptide were examined. Incubation of the synthase *apoenzyme* with trypsin (3.6% w/w) resulted in the time-dependent coordinate loss (75% at 1 h) of both enzymatic activities and the cleavage (85...

... synthase. Two reversible cyclooxygenase inhibitors, ibuprofen and flufenamate, also made both of the activities and the synthase polypeptide more resistant to trypsin. Titration of the *apoenzyme* with indomethacin (0-3 mol/mol of synthase dimer) resulted in proportional increases in the

inhibition of the cyclooxygenase and in the resistance to attack...

... interaction of these agents with the synthase that produced inhibition of the cyclooxygenase led to a decreased accessibility of the Arg253 region to proteases. Aspirin *treatment* made the synthase less resistant to trypsin; aspirin-treated synthase became more resistant to trypsin when it was incubated with indomethacin before addition of the protease. The presence of 50 microM arachidonate during digestion of *apoenzyme* or aspirin-treated *apoenzyme* with trypsin did not decrease the cleavage of the synthase subunit.(ABSTRACT *TRUNCATED* AT 400 WORDS)

9/3,K/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08192297 PMID: 2500968
Differential labeling of the catalytic subunit of cAMP-dependent protein kinase with acetic anhydride: substrate-induced conformational changes.
Buechler J A; Vedvick T A; Taylor S S
Department of Chemistry, University of California, San Diego, La Jolla 92093.
Biochemistry (UNITED STATES) Apr 4 1989, 28 (7) p3018-24, ISSN 0006-2960 Journal Code: 0370623
Contract/Grant No.: AM07233; AM; NIADDK; GM19301; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

... to identify regions that are sensitive to substrate-induced perturbations, the catalytic subunit of cAMP-dependent protein kinase was differentially labeled with [3H]acetic anhydride. *Treatment* of the catalytic subunit with acetic anhydride in the absence of substrates led to the irreversible inhibition of activity, and MgATP protected against inactivation. After...
...purification protocol for the lysine-containing peptides, the reactivity of each lysine in the native enzyme was calculated. The reactivity profile of lysines in the *apoenzyme* revealed three distinct regions. In general, the lysines within the amino-terminal segment (residues 1-83) and the carboxy-terminal segment (192-345) were relatively...

... peptide. MgATP affords substantial protection to three residues in particular. Lys-72, predicted previously to be essential for nucleotide binding was relatively reactive in the *apoenzyme*, whereas labeling was nearly abolished in the presence of MgATP.(ABSTRACT *TRUNCATED* AT 250 WORDS)

9/3,K/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08106382 PMID: 2496197
Phytic acid-enhanced metal ion exchange reactions: the effect on carboxypeptidase A.
Martin C J; Evans W J
Department of Biochemistry, Chicago Medical School, University of Health Sciences, Illinois 60064.
Journal of inorganic biochemistry (UNITED STATES) Apr 1989, 35 (4) p267-88, ISSN 0162-0134 Journal Code: 7905788
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

... left after incubation at pH 7.2 for 24 hrs at 25 degrees C, but the

initial activity could not be regained under similar assay *treatment*. An increase in either the Cu(II) or phytate concentration while the other was kept constant, yielded saturation curves with maximal effect at 3 x...

... not only the removal of the zinc ion from the active site but also the sequential and rapid incorporation of a cupric ion into the *apoenzyme* so formed. (ABSTRACT *TRUNCATED* AT 400 WORDS)

9/3,K/14 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07886182 PMID: 3047520
Improved glycemic control lowers plasma apoprotein E and triglyceride levels following ingestion of a fat load in insulin-dependent diabetic subjects.
Georgopoulos A; Applebaum-Bowden D; Margolis S
Department of Medicine, The Johns Hopkins University, School of Medicine, MD 21205.
Metabolism- clinical and experimental (UNITED STATES) Sep 1988, 37 (9) p837-43, ISSN 0026-0495 Journal Code: 0375267
Contract/Grant No.: RR-0003524; RR; NCRR
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

... subjects) or vegetable oil (four subjects). A repeated-measures ANOVA was performed to assess the effects of the following three factors on plasma TG and *apoE* levels: type of oil ingested (Oil, factor A), glycemic control (Glycemic control, factor B), and the response to fat ingestion over time (Times, factor C...
... P less than .05, respectively). The effect of the type of oil and the interactions tested (AB, AC, BC, ABC) were not statistically significant. (ABSTRACT *TRUNCATED* AT 250 WORDS)
; Adult; Diabetes Mellitus, Type I--drug *therapy*--DT; Food; Insulin --administration and dosage--AD; Middle Aged

9/3,K/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06447285 PMID: 6606590
Diabetes-induced metabolic alterations in heme synthesis and degradation and various heme-containing enzymes in female rats.
Bitar M; Weiner M
Diabetes (UNITED STATES) Jan 1984, 33 (1) p37-44, ISSN 0012-1797 Journal Code: 0372763
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

... rats. Animals were rendered diabetic by a single i.v. injection of streptozotocin (STZ, 65 mg/kg) and measurements were made at various times after *treatment* . The basal levels of the key enzymes involved in heme synthesis, ALA-S and ALA-dehydratase (ALA-D), were decreased about 36% and 54%, respectively...

... hydrogenase, the rate-limiting enzyme in corticosterone metabolism, exhibited a 35-65% decrease in activity throughout the experimental period. Tryptophan pyrrolase activity (total, holo-, and *apoenzyme*) was elevated about 2.5-fold in STZ diabetic rats. In vivo insulin *therapy* of diabetic animals antagonized the effect of the diabetic state on the above measured parameters. *Treatment* with aminoglutethimide resulted in about a twofold

elevation in ALA-S activity in control as well as chronically diabetic rats. However, a similar stimulatory response in ALA-S activity to CoCl2 administration was observed only in control or insulin-treated diabetic rats.(ABSTRACT *TRUNCATED* AT 250 WORDS)

9/3,K/16 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013402343 BIOSIS NO.: 200100574182
Vascular-derived thrombin generates neurotoxic apolipoprotein E fragments
AUTHOR: Grammas P (Reprint); Ottman T (Reprint); Reimann-Philipp U (Reprint)
AUTHOR ADDRESS: Oklahoma Center of Neuroscience, University of Oklahoma HSC, Oklahoma City, OK, USA**USA
JOURNAL: Society for Neuroscience Abstracts 27 (2): p2002 2001 2001
MEDIUM: print
CONFERENCE/MEETING: 31st Annual Meeting of the Society for Neuroscience San Diego, California, USA November 10-15, 2001; 20011110
ISSN: 0190-5295
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Neuronal cell loss is a critical component in the pathogenesis of Alzheimer's disease (AD). Inheritance of the *ApoE4* genotype increases the risk of developing AD and *truncated* *ApoE* has been shown to have neurotoxic properties. Also, the serine protease thrombin is elevated in the AD brain and is neurotoxic in vitro. We have...
...expression of inflammatory mediators. The objective of this study was to determine if "activated" brain endothelial cells could be a source of thrombin and neurotoxic *ApoE* fragments. Brain endothelial cells were treated with an inflammatory cocktail containing (IL-1beta, IL-6, LPS, IFNgamma, TNFalpha) for 24 hrs and conditioned media collected. Conditioned media were incubated with *ApoE* for 24 hrs and then analyzed by Western blot for detection of *ApoE* fragments. The results showed that endothelial cell conditioned media generated several *ApoE* fragments (22-26 kDa). This pattern was consistent with that observed using purified thrombin. In addition, thrombin activity was significantly ($p<0.01$) increased in the endothelial cell media after inflammatory *treatment*. Finally, addition of *ApoE* with thrombin to primary cerebral cortical neuronal cultures resulted in higher levels of neuronal cell death than that evoked by either *ApoE* or thrombin alone. These data suggest that endothelial cell activation results in thrombin production and that brain endothelium could be a source of neurotoxic factors...

9/3,K/17 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

10915518 EMBASE No: 2000412833
Recent advances in the analysis of HCV NS5B RNA-dependent RNA polymerase
Lesburg C.A.; Radfar R.; Weber P.C.
C.A. Lesburg, Department of Structural Chemistry, Schering-Plough Research Institute, 2015 Galloping Hill Road, Kenilworth, NJ 07033 United States
AUTHOR EMAIL: Charles.Lesburg@spcorp.com
Current Opinion in Investigational Drugs (CURR. OPIN. INVEST. DRUGS) (United Kingdom) 2000, 1/3 (289-296)
CODEN: CIDRE ISSN: 0967-8298
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 42

...hepatitis C virus genome. Recent advances in the biochemical and structural understanding of NS5B include solubilization and purification of the full-length enzyme and various *truncated* forms. In vitro conditions for NS5B-catalyzed primer elongation using both homo- and heteropolymeric RNA templates were discovered. The crystal structure of the NS5B *apoenzyme* revealed a globular shape unique among polymerases, and implicated new structural features important for binding the RNA template and cognate ribonucleotide substrates. The crystallographic results...
DRUG DESCRIPTORS:
*virus protein--endogenous compound--ec; *RNA directed RNA polymerase --endogenous compound--ec; *antivirus agent--pharmacology--pd; *antivirus agent--drug *therapy*--dt; *antivirus agent--drug analysis--an; * nucleotidyltransferase inhibitor--pharmacology--pd; *nucleotidyltransferase inhibitor--drug analysis--an; *nucleotidyltransferase inhibitor--drug *therapy*--dt
...analysis--an; nucleoside analog--drug analysis--an; benzothiophene derivative--drug analysis--an; butyric acid derivative--drug analysis--an; indole derivative--pharmacology--pd; indole derivative--drug *therapy*--dt; indole derivative--drug analysis--an; unclassified drug
MEDICAL DESCRIPTORS:
...structure; solubilization; enzyme purification; protein analysis; protein expression; enzyme activity; amino acid sequence; virus replication ; protein polymerization; DNA template; antiviral activity; Flavivirus; hepatitis C--drug *therapy*--dt; drug design; experimental model; virus inhibition; review
DRUG TERMS (UNCONTROLLED): RNA directed RNA polymerase inhibitor --pharmacology--pd; RNA directed RNA polymerase inhibitor--drug *therapy* --dt; RNA directed RNA polymerase inhibitor--drug analysis--an; vp 32947 --pharmacology--pd; vp 32947--drug *therapy*--dt; vp 32947--drug analysis --an

9/3,K/18 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

07121865 EMBASE No: 1998012613
Characteristics of cerebral beta amyloid deposition in four non-demented patients in their forties with a high apolipoprotein E epsilon4 allele frequency
Sugihara S.; Saunders A.M.; Ogawa A.; Nakazato Y.; Saido T.C.; Yamaguchi H.
Dr. H. Yamaguchi, Gunma Univ. School Health Sciences, 3-39-15 Showa-machi, Maebashi, Gunma 371 Japan
AUTHOR EMAIL: yamaguti@news.sb.gunma-u.ac.jp
Neuropathology (NEUROPATHOLOGY) (Australia) 1997, 17/4 (326-333)
CODEN: NOPAF ISSN: 0919-6544
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 37

...beta amyloid deposition were examined. Three patients had breast cancer, and in one of these cases it was associated with brain metastasis and brain radiation *therapy*. One other case had pulmonary small cell carcinoma. In two patients, small beta amyloid deposits were only found in the frontal cortex. In another two...
...amyloid beta protein (Abeta), Abeta42 was predominant in the diffuse plaques and immunoreactions for Abeta40 varied among the patients. The N-terminal of Abeta was *truncated* in a subset of plaques. Tau- and phosphorylated tau-reactive fine neurites were only found in the entorhinal cortex of Case 3. The *apoE* genotype of these four patients were 3/4, 3/4, 4/4 and 3/3, and therefore, the epsilon4 allele frequency (50%) was as high ...
?ds

Set	Items	Description
S1	253	(TRUNCATED) (S) (APOE3 OR APOE-3 OR APOE?)

```
S2          22   S1 (S) (VECTOR OR PLASMID OR ADENOVIRUS OR ADENOVIRAL)
S3          14   S2 AND (CHOLESTEROL OR HYPERTRIGLYCERIDEMIA)
S4           6   RD (unique items)
S5           8   S2 NOT S3
S6           5   RD (unique items)
S7          23   S1 AND (TREATMENT OR THERAPY)
S8          20   RD (unique items)
S9          18   S8 NOT S2
?logoff
       13apr04 12:34:23 User259876 Session D610.2
            $3.38    1.058 DialUnits File155
               $4.83  23 Type(s) in Format  3
            $4.83  23 Types
     $8.21  Estimated cost File155
            $2.47    0.440 DialUnits File5
               $7.00  4 Type(s) in Format  3
            $7.00  4 Types
     $9.47  Estimated cost File5
            $8.50    0.867 DialUnits File73
               $5.40  2 Type(s) in Format  3
            $5.40  2 Types
    $13.90  Estimated cost File73
            OneSearch, 3 files,  2.365 DialUnits FileOS
     $2.25  TELNET
    $33.83  Estimated cost this search
    $34.21  Estimated total session cost   2.459 DialUnits


### Status: Signed Off. (10 minutes)
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